NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

*The corresponding author has opted to make this information publicly available.

Personal or nonessential information may be redacted at the editor’s discretion.

Questions about these materials may be directed to the Obstetrics & Gynecology editorial office:

obgyn@greenjournal.org.
Date: Jul 01, 2021
To: "Molly Boyer Broache"
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-1238

RE: Manuscript Number ONG-21-1238

Performance of the BD MAX™ Vaginal Panel assay compared to clinical diagnosis of vaginitis

Dear Dr. Broache:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the referees and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jul 22, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

ABSTRACT
In the concluding section, please be more specific about the effect of the MVP on accuracy. Namely, if this test had been used, how many more patients would have been treated appropriately, and how many more would not have been treated because they were uninfected?

METHODS
1. Please list the centers where this study was conducted. Please provide a brief description of the patient populations at each center.

2. Please specify the length of time required to complete an individual test? In a real-world situation, could this test be easily done in the office, or would it need to be sent to a certified laboratory?

3. Please specify the approximate cost of the test in clinical practice.

RESULTS
For each infection, please list the total number of patients who were not treated correctly, i.e, they tested positive by the MVP but were negative by clinical exam or they had a positive clinical diagnosis but were not truly infected.

DISCUSSION
1. Please provide a reference for your statement that the CDC now specifies the NAAT as the test of choice for trichomonas.

2. Please describe briefly the consequences of failing to treat infected patients and incorrectly treating uninfected patients.

3. Please summarize how you envision using this test in clinical practice. Should it be a point of care test done in the office by the clinician or a test that should be sent to the reference laboratory for a quick turn-around result. If the patient were acutely symptomatic, would you delay treatment until the result of the MVP is known?
Reviewer #2:

Abstract - Objective - vaginitis - BV, yeast, trichomonas - compare BD Max testing to clinical diagnosis
Methods - 5 collections sites, 1 testing site, 469 specimens with 467 BV results and 466 yeast/ trichomonas results
Results - Clinical diagnosis agrees with BD Max 57.9%, 53.5%, 28% for the 3 different types of infection and negative agreement is 80%, 77%, 99.8%
percentage not treated who warranted treatment based on negative clinical diagnosis: 65%, 44%, 55.6%
Conclusions - MVP detected many untreated patients and improved diagnosis

Intro - BDMAX vaginal panel is NAATs, better than clinical diagnosis
Disclosure of sponsors
Materials and Methods - multicenter, prospective, cross-sectional study, sample size to detect 100 of each infection
Objective - compare MVP to clinical diagnosis
Results - 469 tests, BV - positive percent agreement (PPA) - 57.9%, negative percent agreement 80%
Candida - PPA - 53.5%, NPA 77%
Trichomonas - PPA 28% and NPA 99.8%
of MVP positive and clinical diagnosis negative - 65%, 44%, 55.6% had no treatment for each respective infection
Discussion - limiteid accuracy of clinical diagnosis, ACOG and CDC guidelines should recommend molecular based testing without speculum

Comments -
1) What is the mode of collection for the BD Max vaginal panel - it is not mentioned until the very end that it is done without a speculum. Is it always without a speculum? Is it a self collected test? Is it a home test?
2) It is clearly superior to clinical diagnosis, but how does it compare to the widely available vaginosis screen? Is it the same, it is presented here as a novel test - what is different? This clearly illustrates that this test is superior to clinical diagnosis, but what is new/ novel?

Reviewer #3:

This is a multi-center prospective cross-sectional study on the performance of the BD MAX™ Vaginal Panel compared to clinical diagnosis of vaginitis. The authors explain the BD MAX™ Vaginal Panel in detail and give supporting results about improved management of patient with vaginitis when treatment is based on results of the BD MAX™ Vaginal Panel rather than clinical diagnosis in a routine office visit. A key detail that is not included is the test result turnaround time. The authors do not state if the BD MAX™ Vaginal Panel can be performed in the office during the clinical consultation. Line 229-230: Consider supporting this statement with references. Line 232: Consider supporting this statement with references.

STATISTICS EDITOR COMMENTS:

Lines 14-15: The %s and CIs should all be rounded to nearest integer % since the respective denominators were N = 103, 59 and 18.
Table 1: Need units for age.

Tables 2, 3, 4: Need to round Kappa to 0.001 precision and include CIs with same precision limit.

Table 2: The results are more complex that simply comparing the PPA and NPA (ie, the column proportions). If evaluated from the point of view of comparing the clinical diagnosis, then the MVP result (ie, the row proportions), a (+) clinical ddx is associated with a (+) MVP result 63% of the time, while for a (-) clinical dx and a (-) MVP, that proportion is ~ 76%.

Table 3: Comparing the row proportions for VVC, a negative clinical impression was associated with (-) MVP 81% of the time, while a positive clinical impression was associated with a (+) MVP only. In other words, the utility of clinical impression vs MVP result may be dependent on the pathogen.

Table 4: It is difficult to extrapolate these results, since the prevalence of TV was low in this series, hence the CIs for PPA were wide (21%, 49%). In this series, simply diagnosing all as (-) would have been correct > 90% of the time.

Appendix and lines 218-222: There is considerable variability by study site, not just "some variability". For example, using Chi-square to compare OPA rates for BV for the 5 sites, the Chi-square = 35.1, with P < 0.0001. For study site and VVC, the chi-square = 16.2, with p = 0.003. For TV, The Chi-square = 14.4, p = 0.006, but many counts are small and that test may not be as reliable as Fisher's test. In summary, there is considerable variability in the accuracy by site, which could be interpreted as meaning that the accuracy metrics proposed not be applicable to all sites or all clinicians. Need to clarify and explain this variability.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
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2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

   If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also
should be described (e.g., in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women’s Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.
10. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

11. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

12. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%).

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

14. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document.

If the reference you are citing has been updated and replaced by a newer version, please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

15. Figure 1: okay

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.
Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded as a Microsoft Word document. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors' comments.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jul 22, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Associate Editor, Gynecology

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.
8 September 2021

John O. Schorge, MD
Associate Editor, Gynecology
Obstetrics & Gynecology
Tufts University
Boston, MA 02111
USA

Dear Dr. Schorge:

Thank you for the opportunity to submit a revised version of our manuscript, “Performance of the BD MAX™ Vaginal Panel assay compared to clinical diagnosis of vaginitis,” for publication in Obstetrics & Gynecology. We very much appreciate all of the comments and input on this manuscript from each of the reviewers and the editorial team.

Included with this submission, you will find a clean version of the manuscript, a clean version of the manuscript with changes highlighted, and a tracked changes version of the manuscript. Also, a detailed response to each of the reviewer’s suggestions is attached below.

I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Please do not hesitate to contact me if you have any questions regarding this submission. Thank you for the opportunity to submit this manuscript for publication in Obstetrics & Gynecology.

Sincerely,

Stephanie Taylor, MD
Professor of Medicine and Microbiology, Section of Infectious Disease
Louisiana State University, School of Medicine
REVIEWER COMMENTS:

Reviewer #1:

1-1 ABSTRACT
In the concluding section, please be more specific about the effect of the MVP on accuracy. Namely, if this test had been used, how many more patients would have been treated appropriately, and how many more would not have been treated because they were uninfected?

Response:
This information has been added to the Abstract at (~line(s) 15-18 of the tracked, revised manuscript).

Sixty-five percent (67/103), 44% (26/59), and 56% (10/18) of patients identified as having BV, Candida spp., and TV by MVP, respectively, were not treated for vaginitis based on a negative clinical diagnosis. Compared to MVP, clinical diagnosis had false positive rates of 19.8%, 23.0%, and 0.2% for BV, Candida spp., and TV, respectively.

A sentence was deleted in the Abstract to better clarify the overall findings (~line(s) 19-20 of the tracked, revised manuscript).

METHODS
1-2 Please list the centers where this study was conducted. Please provide a brief description of the patient populations at each center.

Response:
Please see Appendices 2 and 3.

1-3 Please specify the length of time required to complete an individual test? In a real-world situation, could this test be easily done in the office, or would it need to be sent to a certified laboratory?

Response:
The BD MAX Vaginal Panel assay takes approximately 3 hours to run on the BD MAX instrument, and between 2 and 24 samples can be run simultaneously on the BD MAX. The BD MAX instrument is used in physician office labs as well as reference labs. This is a CLIA moderately complex system. This information is now included in the Discussion (~line(s) 255-257 of the tracked, revised manuscript).

1-4 Please specify the approximate cost of the test in clinical practice.

Response:
The specific cost is not possible to report since this is influenced by the purchasing agreement of various institutions with suppliers, the local costs for laboratory personnel and the various overhead costs incurred in different clinical settings.

RESULTS

1-5 For each infection, please list the total number of patients who were not treated correctly, i.e., they tested positive by the MVP but were negative by clinical exam or they had a positive clinical diagnosis but were not truly infected.

Response:
The information is in the Results (~line(s) 158, 165-166, 173, and 177-181 of the tracked, revised manuscript).

DISCUSSION

1-6 Please provide a reference for your statement that the CDC now specifies the NAAT as the test of choice for trichomonas.

Response:
Based on the most recent guidelines (Workowski, K. A., et al. 2021 Sexually Transmitted Infections Treatment Guidelines, 2021. Mmwr Recommendations and Reports 70(4):1-190), released last week, we need to revise this language. The following language:

Nucleic acid amplification tests (NAATs) are recommended as the laboratory reference standard for detection of *Trichomonas vaginalis*. {Workowski, 2015 #2377}

Replaced:
Recent CDC guidelines state that NAATs have a high sensitivity for detection of *Trichomonas vaginalis* TV, compared to wet mount microscopy. {Workowski, 2021 #10892}

In the first paragraph of the Introduction (~line(s) 31-33 of the tracked, revised manuscript).

The following language was inserted in paragraph 5 of the Discussion (~line(s) 245-2246 of the tracked, revised manuscript).

In addition, NAAT testing is generally accepted as a more sensitive diagnostic approach for TV detection than wet mount microscopy. {Workowski, 2021 #10892}

1-7 Please describe briefly the consequences of failing to treat infected patients and incorrectly treating uninfected patients.

Response:
Additionally, women with untreated trichomonas, which is common with co-infections with BV that receive treatment only for BV, have been shown to be at substantially increased risk for HIV acquisition Mavedzenge, S. N., et al. 2010 Epidemiological synergy of Trichomonas vaginalis and HIV in Zimbabwean and South African women. Sex Transm Dis 37(7):460-6). Conversely, broader treatment without knowing infection status is discouraged for all infectious diseases due to the risk of enabling development of antimicrobial resistance.

1-8 Please summarize how you envision using this test in clinical practice. Should it be a point of care test done in the office by the clinician or a test that should be sent to the reference laboratory for a quick turn-around result. If the patient were acutely symptomatic, would you delay treatment until the result of the MVP is known?

Response:
As described in the response to question 1-3, the BD MAX Vaginal Panel takes approximately 3 hours to run on the BD MAX instrument. If a physician office has a BD MAX instrument in their office, they can likely provide a patient with a same-day result. If the physician is sending the sample to a reference lab, the turn-around time may be approximately 24-72 hours, dependent on several factors (location, lab volume, availability of courier services). The recommendation for symptomatic patients would be to wait for a result to return before prescribing treatment; as this paper shows, assessment and treatment based on in-office assessment often leads to an incorrect treatment.

This information is now incorporated into paragraph 5 of the Discussion (~line(s) 257-260 of the tracked, revised manuscript).
Reviewer #2:

Abstract - Objective - vaginitis - BV, yeast, trichomonas - compare BD Max testing to clinical diagnosis Methods - 5 collections sites, 1 testing site, 469 specimens with 467 BV results and 466 yeast/ trichomonas results Results - Clinical diagnosis agrees with BD Max 57.9%, 53.5%, 28% for the 3 different types of infection and negative agreement is 80%, 77%, 99.8% percentage not treated who warranted treatment based on negative clinical diagnosis: 65%, 44%, 55.6% Conclusions - MVP detected many untreated patients and improved diagnosis

Intro - BDMAX vaginal panel is NAATs, better than clinical diagnosis Disclosure of sponsors Materials and Methods - multicenter, prospective, cross-sectional study, sample size to detect 100 of each infection Objective - compare MVP to clinical diagnosis Results - 469 tests, BV - positive percent agreement (PPA) - 57.9%, negative percent agreement 80% Candida - PPA - 53.5%, NPA 77% Trichomonas - PPA 28% and NPA 99.8% of MVP positive and clinical diagnosis negative - 65%, 44%, 55.6% had no treatment for each respective infection Discussion - limited accuracy of clinical diagnosis, ACOG and CDC guidelines should recommend molecular based testing without speculum

Comments -
2-1 What is the mode of collection for the BD Max vaginal panel - it is not mentioned until the very end that it is done without a speculum. Is it always without a speculum? Is it a self collected test? Is it a home test?

Response:
To collect the BD MAX Vaginal Panel, clinicians use the BD MAX UVE Collection Kit, which includes a swab and a sample buffer tube in which the swab is inserted. This swab can be collected by a healthcare provider or by the patient (self-collection must occur in a clinical setting). It is not a home test. This test is intended for patients who present to the clinic with symptoms consistent with vaginitis.

This information is now included in the Materials and Methods (~line(s) 109-114 of the tracked, revised manuscript).

For clinician collection, a speculum could be used if the provider desires to use one, but it is not necessary. BD provides collection instructions to providers that indicate how collection can be done with and without the assistance of a speculum.

2-2 It is clearly superior to clinical diagnosis, but how does it compare to the widely available vaginosis screen? Is it the same, it is presented here as a novel test - what is different? This clearly illustrates that this test is superior to clinical diagnosis, but what is new/ novel?

Response:
The following is a description of MVP in comparison to Affirm for some aspects of clinical application. The authors are willing to update the manuscript, further, based on this language or further input from the Reviewer.
Some of the advantages for utilization of MVP include: improved detection of conditions through use of NAAT technology (Affirm uses DNA probe-based technology), ability to offer a self-collected or clinician collected specimen (Affirm only offers clinician collection), the ability to call out Candida glabrata and Candida krusei separately (these are included within a group call in the Affirm panel, however, there is a benefit to separating out Candida glabrata and Candida krusei since they may have resistance to azole medications), detection of Trichomonas vaginalis through NAAT—less hands on time and manual manipulation per sample, ability to run 24 samples per 3 hours (affirm is six samples in approximately 45 minutes).
Reviewer #3:

This is a multi-center prospective cross-sectional study on the performance of the BD MAX™ Vaginal Panel compared to clinical diagnosis of vaginitis. The authors explain the BD MAX™ Vaginal Panel in detail and give supporting results about improved management of patient with vaginitis when treatment is based on results of the BD MAX™ Vaginal Panel rather than clinical diagnosis in a routine office visit.

3-1 A key detail that is not included is the test result turnaround time. The authors do not state if the BD MAX™ Vaginal Panel can be performed in the office during the clinical consultation.

Response:
As described above (R1:C3, R1:C8), the BD MAX Vaginal Panel takes approximately 3 hours to run on the BD MAX instrument. If a physician office has a BD MAX instrument in their office, they can likely provide a patient with a same-day result. If the physician is sending the sample to a reference lab, the turn-around time may be approximately 24-72 hours, dependent on several factors (location, lab volume, availability of courier services). The recommendation for symptomatic patients would be to wait for a result to return before prescribing treatment; as this paper shows, assessment and treatment based on in-office assessment often leads to an incorrect treatment.

This information is now incorporated into paragraph 5 of the Discussion (~line(s) 255-257 of the tracked, revised manuscript).

3-2 Line 229-230: Consider supporting this statement with references.

Response: This has been done (~line(s) 278 of the tracked, revised manuscript).


3-3 Line 232: Consider supporting this statement with references.

Response: This statement was an oversight on our part and has been removed. We apologize for any confusion or inconvenience.
STATISTICS EDITOR COMMENTS:

SE-1 Lines 14-15: The %s and CIs should all be rounded to nearest integer % since the respective denominators were N = 103, 59 and 18.

Response:
This has been done (~line(s) 15 of the tracked, revised manuscript).

SE-2 Table 1: Need units for age.

Response:
This has been done at Table 1.

SE-3 Tables 2,3,4: Need to round Kappa to 0.001 precision and include CIs with same precision limit.

Response:
This has been done in Tables 2, 3, 4, and Appendix 4.

SE-4 Table 2: The results are more complex that simply comparing the PPA and NPA (ie, the column proportions). If evaluated from the point of view of comparing the clinical diagnosis, then the MVP result (ie, the row proportions), a (+) clinical ddx is associated with a (+) MVP result 63% [Authors’ note: should be reversed with 76% below?] of the time, while for a (-) clinical dx and a (-) MVP, that proportion is ~ 76%.

Response:
We understand this comment, and agree, to a certain extent, with the main point. However, we believe that the false negative rate (42.0%) holds greater clinical relevance here as it reflects that number of missed positive cases by clinical diagnosis as compared to MVP. The false positive rate (23.7%) is lower than the false negative rate, but it does not result in infected individuals going untreated.

SE-5 Table 3: Comparing the row proportions for VVC, a negative clinical impression was associated with (-) MVP 81% of the time, while a positive clinical impression was associated with a (+) MVP only [Authors’ note: 46.5% of the time?]. In other words, the utility of clinical impression vs MVP result may be dependent on the pathogen.

Response:
We agree that the utility of clinical impression vs MVP may be pathogen dependent.

SE-6 Table 4: It is difficult to extrapolate these results, since the prevalence of TV was low in this series, hence the CIs for PPA were wide (21%, 49%). In this series, simply diagnosing all as (-) would have been correct > 90% of the time.

Response:
We agree with the Statistical Editor. We have included new language in the Discussion (~line(s) 220-223 of the tracked, revised manuscript).
‘The low prevalence of TV (as identified by MVP, the reference method) here resulted in a low group number of total TV positive and probably restricted our ability to obtain a completely unbiased assessment of clinician diagnosis; which is reflected in the wide 95% confidence interval (21.0%, 49.0%). Regardless, the real-world data shown here further highlight the low sensitivity for detection associated with the TV cause of vaginitis.’

SE-7 Appendix and lines 218-222: There is considerable variability by study site, not just "some variability". For example, using Chi-square to compare OPA rates for BV for the 5 sites, the Chi-square = 35.1, with P < 0.0001. For study site and VVC, the chi-square = 16.2, with p = 0.003. For TV, The Chi-square = 14.4, p = 0.006, but many counts are small and that test may not be as reliable as Fisher's test. In summary, there is considerable variability in the accuracy by site, which could be interpreted as meaning that the accuracy metrics proposed not be applicable to all sites or all clinicians. Need to clarify and explain this variability.

Response:
The following language is now included in the Discussion (~line(s) 262-266 of the tracked, revised manuscript).

There is extensive variability in the accuracy of clinical diagnosis, compared to MVP, when data is analyzed by study site (Appendix 3). This could have occurred as a result of demographic make-up, standard operating procedure, variation from site to site, differences in age of the populations, and the inclusion of some sites with low sample size, among other reasons.
EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
   A. OPT-IN: Yes, please publish my point-by-point response letter.
   B. OPT-OUT: No, please do not publish my point-by-point response letter.

Response:
A. OPT-IN: No, please do not publish my point-by-point response letter.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

Response:
Yes, we will.

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

Response:
Done.

4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.
Response: This has been done in the Materials and Methods (~line(s) 92-96 of the tracked, revised manuscript).

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

Response:
This has been done throughout the manuscript.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions__;!!AMCWqqRr6m4Wx4!AVvt5mTelaWHM0vxFwUqOnYDBZCJr1hXXYvLuZyk8KNaYhuUR2cAiJUL6kWAVK6$ and the gynecology data definitions at https://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions__;!!AMCWqqRr6m4Wx4!AVvt5mTelaWHM0vxFwUqOnYDBZCJr1hXXYvLuZyk8KNaYhuUR2cAiJUL0m895Sv$. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response:
Done.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

Response:
Within limit.

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

**Response:**
Done.

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

**Response:**
It is around 250 words.

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://urldefense.com/v3/__http://edmgr.ovid.com/ong/accounts/abbreviations.pdf__;!!AMCWqqRremt4Wx4!AVvt5mTeaWHM0vxFwUqOnYDBZCJr1hXXYvLuZyk8KNaBYhuUR2cAiJUL4a2Gb5H$ . Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

**Response:**
Done.

10. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

**Response:**
Done.
11. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which you are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

Response:
Done.

12. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1").

Response:
Noted.

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: https://urldefense.com/v3/__http://edmgr.ovid.com/ong/accounts/table_checklist.pdf__;!!AMCWqqRremt4Wx4!AVvt5mTeiWHM0xuFwUqOnYDBZCJr1hXXYvLuZyk8KNaBYhuUR2cAiJUL3PmtJA1$.

Response:
Done.

14. Please review examples of our current reference style at https://urldefense.com/v3/__http://ong.editorialmanager.com__;!!AMCWqqRremt4Wx4!AVvt5mTeiWHM0xuFwUqOnYDBZCJr1hXXYvLuZyk8KNaBYhuUR2cAiJULyZqqLx$I (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised
versions. If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at https://urldefense.com/v3/__https://www.acog.org/clinical__;!!AMCWqqRremt4Wx4!AVvt5mTeaWHM0vxuQonYDBZCjrhXXYvLuZyk8KnBYhuUR2caJUL8izLloPS (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document.

If the reference you are citing has been updated and replaced by a newer version, please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Response:
Done.

15. Figure 1: okay

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

Response:
Done.

16. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at https://urldefense.com/v3/__http://links.lww.com/LWW-
If your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

If you choose open access, you will receive an Open Access Publication Charge letter from the Journal's Publisher, Wolters Kluwer, and instructions on how to submit any open access charges. The email will be from publicationservices@copyright.com with the subject line, "Please Submit Your Open Access Article Publication Charge(s)." Please complete payment of the Open Access charges within 48 hours of receipt.

Response:
Acknowledged.
RE: Manuscript Number ONG-21-1238R1

Performance of the BD MAX™ Vaginal Panel assay compared to clinical diagnosis of vaginitis

Dear Dr. Broache:

Your manuscript has been reviewed by our editors and they would like your response to further queries and edits.

Below you will find the comments and queries we would like addressed. Emily Fernandez, our Editorial Assistant (efernandez@greenjournal.org), will be sending a Word document copy of your paper. Please make all edits to this version of the paper and submit via Editorial Manager when you are done. Please be sure to address all comments in your point-by-point response. Do not turn off track changes or approve any changes and do not delete comments or resolve them.

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Aug 18, 2021, we will assume you wish to withdraw the manuscript from further consideration.

COMMENTS:

1. Title: The journal does not use brand names in the title, so the title was reworded. Do you agree with this change?

2. The following co-author(s) will need to complete our electronic Copyright Transfer Agreement, which was sent to them by email through Editorial Manager. Please note their email address(es) and make sure they are correct. Once the form is complete, please add their disclosures to the "Financial Disclosure" section: Karen Eckert (karen_eckert@bd.com).

3. Do you approve the edited running title? We avoid brand names in the running title, so it was reworded.

4. Please confirm with your co-authors whether the edited Financial Disclosure is complete and correct. Edits were made based on what was provided in our Copyright Transfer Agreement.

5. Precis: A generic term must be used in the precis. Is "a vaginal panel assay" okay?

6. Abstract: Please replace "BD MAX Vaginal Panel" and "MVP" in the abstract with a generic, spelled-out phrase ("a vaginal panel assay").

7. Please expand "UVE."

8. Please add some description of stat methods.

9. Introduction: Please replace the text highlighted here with a generic term. Then, replace “BD MAX Vaginal Panel” with that generic term throughout the rest of the paper. Journal style allows the brand name to be mentioned once in the manuscript body text. Do not use the abbreviation "MVP."


11. Results: Please express this p-value and all the p-values in your paper to no more than three decimal places.

12. Discussion: Please expand the abbreviation "VVC" throughout your paper.

13. Already mentioned earlier in Discussion. Do you agree with this change?

14. Consider adding a short paragraph to interpret the (negative?) findings for Candida spp.

15. Already mentioned earlier in Discussion. Do you agree with this change?

16. Not clear what argument is being made here – the authors do not suggest the clinicians here were better at clinical diagnosis, yet make unsupported claim that they performed better than expected. This reads as a digression from the
main findings. Please edit for clarity.

17. Table 5: The editor also would like to move Tables 5-7 to supplemental digital content. Do you agree with this change?

Please let us know if you have any questions!

***

If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded as a Microsoft Word document. Your revision’s cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors’ comments.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Aug 18, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editorial Office of Obstetrics & Gynecology

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.
Dear Dr. Schorge:

Thank you for the opportunity to submit a revised version of this manuscript, “Performance of a Vaginal Panel Assay Compared With the Clinical Diagnosis of Vaginitis,” for publication in Obstetrics & Gynecology. Included with this submission, you will find a tracked version of the manuscript and a clean version of the manuscript with the second-round changes, highlighted in yellow. Also, a detailed response to each of the comments is attached below.

I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Please do not hesitate to contact me if you have any questions regarding this submission. Thank you for the opportunity to submit this manuscript for publication in Obstetrics & Gynecology.

Sincerely,

Stephanie Taylor, MD
Professor of Medicine and Microbiology, Section of Infectious Disease

Louisiana State University, School of Medicine
MANUSCRIPT COMMENTS:

1. Title: The journal does not use brand names in the title, so the title was reworded. Do you agree with this change?

Author response:
This is fine, thank you.

2. The following co-author(s) will need to complete our electronic Copyright Transfer Agreement, which was sent to them by email through Editorial Manager. Please note their email address(es) and make sure they are correct. Once the form is complete, please add their disclosures to the “Financial Disclosure” section: Karen Eckert

Author response:
This has been done.

3. Do you approve the edited running title? We avoid brand names in the running title, so it was reworded.

Author response:
We suggest the following running title:
“Vaginal Panel Assay vs Clinical Diagnosis” to preclude “Vaginal Panel Assay vs Vaginitis Diagnosis.”

4. Please confirm with your co-authors whether the edited Financial Disclosure is complete and correct. Edits were made based on what was provided in our Copyright Transfer Agreement.

Author response:
This has been confirmed.

5. Precis: A generic term must be used in the precis. Is “a vaginal panel assay” okay? Yes

Author response:
This is fine, thank you.

6. Abstract: Please replace “BD MAX Vaginal Panel” and “MVP” in the abstract with a generic, spelled-out phrase (“a vaginal panel assay”?). Let’s use vaginal panel assay through

Author response:
“vaginal panel assay” will now be used throughout the manuscript.
7. Please expand “UVE.”

Author response:
We propose the use of vaginal swab throughout the manuscript. Please see paragraph three of the Methods (line 119). Here we propose to call out the brand name: BD MAX UVE Specimen Collection Swab once, here, vaginal swab will be used thereafter.

8. Please add some description of stat methods.

Author response:
The following language has been added in the Abstract at lines 12-15 (tracked version):
Outcome measures include positive, negative, and overall percent agreement (and accompanying 95% confidence intervals) of clinical assessment with the vaginal panel assay. Inter-rater agreement between the two diagnostic approaches was determined using Cohen’s kappa coefficient.

9. Introduction: Please replace the text highlighted here with a generic term. Then, replace “BD MAX Vaginal Panel” with that generic term throughout the rest of the paper. Journal style allows the brand name to be mentioned once in the manuscript body text. Do not use the abbreviation “MVP.”

Author response:
This is fine and has been done.


Author response:
These results are part of a larger study that utilized three other swab/specimen types. The UVE swab and collection kit was obtained in a randomized fashion with respect to the other collection types.

The use of randomization to describe the methodology for this study is not applicable and should be removed. It was removed from the Methods and Materials at lines 124-125 (tracked version) of the manuscript.

11. Results: Please express this p-value and all the p-values in your paper to no more than three decimal places.

Author response:
These revisions have been incorporated.
12. Discussion: Please expand the abbreviation "VVC" throughout your paper.

Author response:
Vulvovaginal candidiasis now replaces VVC throughout the manuscript

13. Already mentioned earlier in Discussion. Do you agree with this change?

Author response:
This is fine, thank you.

14. Consider adding a short paragraph to interpret the (negative?) findings for Candida spp.

Author response:
Please see the new language in the Discussion (~lines 242-249; tracked version)

15. Already mentioned earlier in Discussion. Do you agree with this change?

Author response:
This is fine, thank you

16. Not clear what argument is being made here – the authors do not suggest the clinicians here were better at clinical diagnosis, yet make unsupported claim that they performed better than expected. This reads as a digression from the main findings. Please edit for clarity.

Author response:
Please see the new language in the Discussion (~lines 299-323; tracked version)

17. Table 5: The editor also would like to move Tables 5-7 to supplemental digital content. Do you agree with this change?

Author response:
This is fine, thank you. We have revised the call-outs in the manuscript for Tables 5-7 to now state Appendices 2-4, respectively. The current Appendices 2-4 are now Appendices 5-7, and all of the call-outs for those have been revised in the manuscript. Appendix 1 remains unchanged, as it is called out earlier than Appendix 2 (previous Table 5).